REMARKS

Claims 6 to 28 are pending.

Claims 1 to 5 are canceled.

Claims 6 to 8, 10, and 13 to 28 were previously presented.

No claims are amended in this paper.

Claim Rejections - 35 U.S.C. § 103

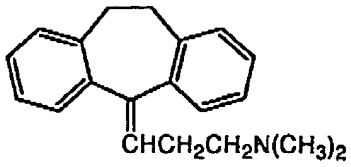
In the Office Action, Claims 6 to 28 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Scherle et al. (The Journal of Immunology, 1998;161:5681-5686) and McGilvray et al. (The Journal of Biological Chemistry, 1997;272(15):10287-10294) in view of Robbins' Pathologic Basis of Disease, 5th ed., 1994, pages 1249-1253, and Bridges (WO 98/37881). It was argued in the Office Action that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the MEK inhibitors of Bridges to treat arthritis such as osteoarthritis and rheumatoid arthritis. Allegedly, the skilled artisan, possessing the teachings of the art cited above, would employ any known MEK inhibitors, including the MEK inhibitors of Bridges, to inhibit production of certain proinflammatory mediators (i.e., IL-1 and TNF-α) and treat rheumatoid arthritis and osteoarthritis, absent evidence to the contrary.

Applicants respectfully traverse the rejection because they believe that the skilled artisan, at the time the present invention was made, would not have had a reasonable expectation of success for practicing the method of the present invention. Applicants believe that a reasonable expectation of success is absent because of the structural dissimilarity between the instant active compounds and the compounds of Scherle et al. and McGilvray et al. when viewed in the context of MPEP § 2143.02.

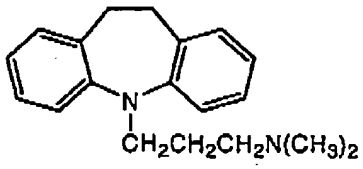
In the MPEP § 2143.02, the context for establishing a reasonable expectation of success for a method of treating a disease seems to be *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicants believe that the court in *In re Merck* relied on the following teachings or suggestions in the prior art to establish that the skilled artisan would have had a reasonable expectation of success for treating depression with amitriptyline: (i) the structurally similar relationship between the prior art compound (imipramine), a known antidepressant, and the compound (amitriptyline) of Merck's invention method of treating depression, (ii) prior art ("Roche Reports") that recognized the structural relationship between imipramine and amitriptyline and concluded that amitriptyline should be tested for antidepressant activity, and (iii)

the bioisosteric relationship between functional groups of imipramine and functional groups of amitriptyline.

The structures of amitriptyline and imipramine, as drawn in 231 USPQ 376, are shown below for reference:



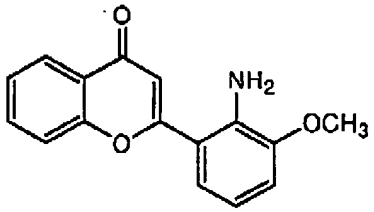
amitriptyline



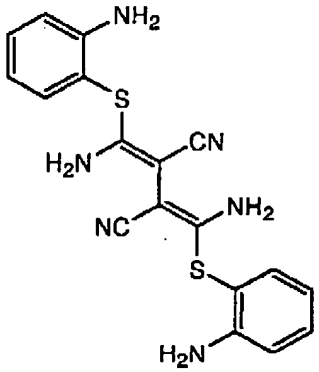
imipramine

Regarding the present rejection, Scherle et al. refer to the MEK inhibitors U0126 and PD98059. Scherle et al. also refer to an inactive analog of U0126, namely U0124. McGilvray refer to the MEK inhibitor, PD98059.

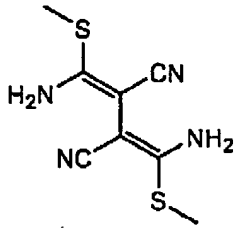
The structures of PD98059, U0126, and U0124, as shown on page 18626 of citation 31 in Scherle et al. (i.e., Favata, Margaret F., et al., J. Biol. Chem., 1998;273(29):18623-18632), and are reproduced below:



PD98059



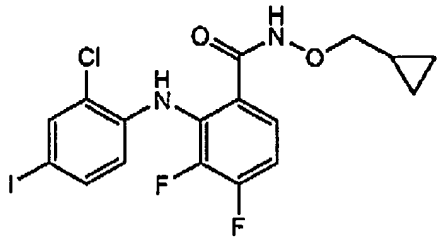
U0126, and



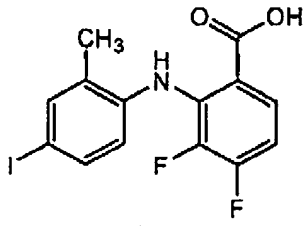
U0124

The compounds U0126 and PD98059 contain H_2N-phenyl moieties, whereas the inactive compound U0124 does not contain an H_2N-phenyl moiety. Applicants believe Scherle et al. teach that structural changes can lead to loss of biological activity.

The structures of the active MEK inhibitors of Formulas I or II of the present claims are not similar to the structures of U0126 or PD98059. For example, instant claim 17 discloses a compound of instant formula II, 2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide, also known as PD 184352, and the instant specification (page 5, line 8) discloses a compound of instant formula I, 3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid (referred to herein as Compound (A)):



PD 184352



Compound (A)

Further, the substituted-diphenylamino functional groups of instant formulas I and II do not have a bioisosteric relationship to functional groups in the compound, PD98059 or U0126.

Applicants believe that Bridges does not cure the deficiencies of Scherle et al. and McGilvray et al. because the structures of the MEK inhibitors of Bridges are not similar to, and do

not have a bioisosteric relationship to, the structures of U0126 or PD98059. Robbins does not cure the deficiencies of Scherle et al. and McGilvray et al. in view of Bridges because Robbins provides no information about MEK inhibitors or structures thereof.

In view of MPEP § 2143.02 and the structure-activity teaching of Scherle et al., Applicants believe that the skilled artisan, at the time of filing the present application, would not have had a reasonable expectation of success for the present invention. Accordingly, Applicants believe that claims 6 to 28 are not obvious over Scherle et al. and McGilvray et al. in view of Robbins and Bridges, and are patentable under 35 U.S.C. § 103(a).

Conclusion

In view of the above amendments and remarks, Applicants believe that the rejection is overcome and request reconsideration of claims 6 to 28.

Respectfully submitted,

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